

**AMENDMENTS TO THE DRAWINGS**

The attached sheet of drawings includes changes to Figure 6.

Exhibit 3: Replacement sheet

### **REMARKS**

Applicants have carefully studied the Office Action dated October 23, 2009, which issued in connection with the above-identified application. The present response is intended to be fully responsive to all points raised by the Examiner and is believed to place the claims in condition for allowance. Favorable reconsideration and allowance of the present claims are respectfully requested.

### **Objection to Drawings**

The Examiner has requested re-submission of Figure 6 to correct illegible axis labels and text legend. Amended Figure 6 is attached herein as Exhibit 3.

### **Objection to the Specification**

The Examiner has requested that the specification is brought in compliance with guidelines concerning the use of trademarks. The specification has been amended to capitalize trademarks. A marked-up copy and a clean copy of the substitute specification containing amendments to the specification are attached herein as Exhibits 1 and 2, respectively. No new matter has been added.

### **Pending Claims**

Claims 1, 2, 6-10, 12, 13, 15, 16, 25, 39, 40, 42-50, 55, 56, 64, 65, 78, 79, 85, 86, 88, 90, 93, 97, and 104 were pending. Claims 55, 56, 90, 93, 97, and 104 have been withdrawn from consideration as being directed to a non-elected invention. The Examiner has rejected each of the examined claims as being anticipated by or obvious over prior art.

By the above amendment to the claims, claims 1, 9, 10, 43, 44 have been canceled without prejudice or disclaimer. Applicants preserve the right to pursue the subject matter of these canceled claims in a continuing application.

Claims 2, 45, 47, 49, 55, 56, 64, 85, 86, 88, 90, 93, 97, and 104 have been amended to specify that the disease or disorder is a neurological, psychiatric or mood disease or disorder. New claim 106 has been added. Support for these amendments and new claim 106 could be found, for example, in paragraphs [0026], [0044], [0052], Example 2 (paragraphs [0124-0142]) and Examples 5-8A (paragraphs [0223-0324]) of the application as published (U.S. Publ. No. 2007/0105105).

Claim 64 has been further amended to recite that step (a) is performed “using the method of claim 2.” Support for this amendment can be found, for example, in Examples 8A and 9 of the present application.

To eliminate any possible ambiguity, claim 13 has been amended to replace the recitation “a neurodegenerative disease or Alzheimer’s disease” with the recitation “a neurodegenerative disease”, because Alzheimer’s disease is a neurodegenerative disease. A new claim 105 which depends from claim 13 and recites Alzheimer’s disease has been added.

Claims 12, 15, 16, 78, 79 have been amended to correct minor typographical errors.

No new matter has been added as a result of these amendments.

#### **Claim Rejections - 35 USC § 102(b)**

Claims 1, 2, 6-10, 39, 40, and 42 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Ralph et al., U.S. Patent No. 6,190,857 (“Ralph”). Claims 1, 2, 6-8, 12, 13, 15, 16, 25, and 44-51 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Ilani et al., Proc. Natl. Acad. Sci. USA, 2001, 98:625-628 (“Ilani”).

As claims 1, 9, 10, and 44 have been canceled, the rejection of these claims is rendered moot.

With respect to the remaining claims and new claims 105 and 106 the rejection is respectfully traversed.

By the present amendment to the claims, all rejected claims are directed to evaluating neurological, psychiatric or mood diseases or disorders. In contrast to the present claims, Ralph does not disclose or suggest evaluating neurological, psychiatric or mood diseases or disorders.

Claims 2, 45, 47, 49, and 106 also recite “comparing an expression profile.” As defined in paragraph [0045] of the present application as published, “[t]he term ‘expression profile’ refers to expression of two or more, preferably three or more, for example 5, 10, 20, 50, 100, 500, or 1000 or more, genes/EST or other transcribed nucleic acids” (emphasis added). All other rejected claims depend directly or indirectly from claims 2, 45, 47, or 49. Thus, the rejected claims are directed to detecting expression of two or more transcribed nucleic acids. In contrast to the present claims, Ilani discloses detecting expression of a single gene, D3 dopamine receptor, and does not disclose or suggest detecting expression of any additional genes.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). See also MPEP § 2131.02.

In view of the foregoing arguments and standards, applicants respectfully submit that the present claims as amended are not anticipated by the cited references and request that the anticipation rejection be withdrawn.

### **Claim Rejections - 35 U.S.C. §103**

The Examiner has rejected claims 64, 65, 78, 79, 85, 86, and 88 as obvious over Kamizono et al., U.S. Patent No. 6,248,533 (“Kamizono”) in view of Ralph and Ilani.

The rejection is respectfully traversed.

Claim 64 as amended recites that step (a) (i.e., selecting a nucleic acid that has altered expression in a surrogate cell from a subject with the disease or disorder, when compared to a surrogate cell from a normal subject or subjects) is performed using the method of claim 2.

The method of claim 2 as amended involves evaluating neurological, psychiatric or mood diseases or disorders by comparing an expression profile of surrogate cells from afflicted and control subjects. As defined in paragraph [0045] of the present application as published, “[t]he term ‘expression profile’ refers to expression of two or more, preferably three or more, for example 5, 10, 20, 50, 100, 500, or 1000 or more, genes/EST or other transcribed nucleic acids” (emphasis added).

Neither Ralph nor Kamizono disclose or suggest that their disclosed methods are applicable to evaluating neurological, psychiatric or mood diseases or disorders. Ilani discloses a connection between schizophrenia and lymphocyte expression of a single gene, D3 dopamine receptor, but does not disclose or suggest that monitoring expression of more than one gene may be needed or useful for disease evaluation.

Detection of expression of multiple transcribed nucleic acids recited in claim 2 provides a significant and unexpected improvement in specificity and accuracy of evaluation of neurological, psychiatric and mood diseases as compared to evaluations based on detecting expression of a single gene (e.g., as disclosed in Ilani). In fact, as disclosed in Example 2 of the present application (see, in particular, Table 2 and paragraph [0136]), D3 dopamine receptor expression was not as statistically significantly different between subjects having schizophrenia and control subjects as expression of many other genes detected by the method of the present invention (e.g., N-CAM, GABA-A receptor, Ciliary neurotrophic factor, etc.). It follows that claim 64 which includes the method of claim 2 is not obvious over the cited references.

Further, step (b) of claim 64 calls for “comparing the sequence of the nucleic acid, including the entire transcribed region, plus upstream and downstream controlling elements, from the subject with disease or disorder and the normal subject or subjects.”

There is nothing in Kamizono to suggest “comparing the sequence of the nucleic acid, including the entire transcribed region, plus upstream and downstream controlling elements, from the subject with the disease or disorder and the normal subject or subjects.” Kamizono merely discloses determining the presence or absence of previously-identified polymorphisms in 5’ flanking regions and certain alleles. Nor is there any disclosure in Ralph or Ilani that would suggest such a comparison. In the absence of a disclosure or suggestion to make a comparison of the entire transcribed and flanking regions, claim 64 is not obvious over Kamizono in view of Ralph and Ilani.

Claims 65, 78, 79, 85, 86, and 88 depend either directly or indirectly from claim 64 and thus include all of the features of claim 64. These additional claims are thus also not obvious over Kamizono in view of Ralph and Ilani, for at least the same reason that claim 64 is not obvious over these references.

With final regard to the obviousness rejection, in discussing Kamizono the Examiner refers to claims 1, 2, 43 and 44 (Office Action at page 7) and in discussing Ralph the Examiner refers to claims 89-94 (Office Action at page 8). Claims 1, 2, 43 and 44, however, are not included in the rejection and claims 89-94 have been either cancelled or withdrawn. The Examiner’s reference to claims 1, 2, 43, 44 and 89-94 thus appears to be extraneous to the obviousness rejection and is not addressed herein.

In light of the above arguments, withdrawal of the obviousness rejection is respectfully requested.

### **CONCLUSION**

Applicants request entry of the foregoing amendments and remarks in the file history of this application. In view of the above arguments, it is respectfully submitted that the present claims are now in condition for allowance and such action is earnestly solicited.

If the Examiner believes that a telephone conversation would help advance the prosecution in this case, the Examiner is respectfully requested to call the undersigned attorney at

(212) 527-7634. The Examiner is hereby authorized to charge any additional fees or credit any overpayment associated with this response to our Deposit Account No. 04-0100.

Dated: February 23, 2010

Respectfully submitted,

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# EXHIBIT- 3

Figure 6 – Replacement Sheet